

A STUDY OF THERMIC FEVER, WITH SPECIAL REFERENCE TO THE BLOOD AND URINE CHEMICAL FINDINGS.

By R. B. H. GRADWOHL, M.D.,

AND

EDWIN SCHISLER, M.D.,

ST. LOUIS, MO.

(From the Chemical Department of the Gradwohl Biological Laboratories and the Medical Wards of the St. Louis City Hospital.)

THERMIC fever is a term applied to certain symptom-complexes that are the result of disturbances of heat regulation, primarily from physical causes, the heat and water content of the air about the body, the condition of the peripheral vascular circulation, etc.; but these causes lead to chemical changes in the organism which are manifested in the characteristic clinical symptoms (auto-intoxication and retention) which, for a matter of classification, we would divide into two classes, namely, mild (due to overwork, bad ventilation, anxiety, worry, uncleanness) and the severe (due to excesses, such as overeating and alcoholism). The causes of all are obviously the same. From a clinical stand-point we call those "mild" cases which reach a temperature of 107° or under and "severe" those which go above that point.

Taking the whole series of cases which may be included in the group, sunstroke and those due to heat prostration which occur in the absence of direct sunlight, we may state that insolation may occur under any circumstances in which heat accumulates in the body, and in which the body does not rid itself of its metabolic end-products such as urea, nitrogen, creatinin, and uric acid.

Hirsch¹ believed that while heat was the primary factor the immediate cause of the trouble was diminution of oxygen and retention of toxic principles. Vincent² also states his belief in a toxic basis. Gordon³ says that recent work tends to the conception of paralyzing action on the nervous system of some toxic element which produces metabolic changes in the neurons, and according to the degree of auto-intoxication the effect of the sunstroke will be either an attack of ordinary heat-prostration or syncope, with unconsciousness or death.

If this be true, then insolation is an auto-intoxication brought about by substances formed in the body under abnormal conditions of heat retention as shown in our findings below. We wish in our figures on blood chemical changes to particularly emphasize the

¹ Quoted by Gordon: Osler, *Modern Medicine*, 1907, i, 52.

² *Ibid.*

³ Osler: *Modern Medicine*, 1907, i, 52 (and R. G. Pearce, xvii, 525).

undue retention in these cases of the non-nitrogenous constituents of proteid metabolism.

The following cases occurred in the service of one of us (Schisler) in the St. Louis City Hospital.

CLINICAL HISTORIES AND LABORATORY DATA.

Evans: male; aged fifty years; brewery worker; habits irregular; entered 5.30 P.M. August 5, 1916; unconscious; temperature, 110.4° (rectal); pulse, 130; respiration, 36; pupils contracted, reaction to light negative; general spasticity of body present; knee-jerks increased; toe signs questionable. The average blood-pressure taken during observation was systolic 91, diastolic 46 (Tycos); 30 c.c. spinal fluid (under normal pressure) was negative (Wassermann); urine albumin +++; many granular and pus casts. The man developed several generalized convulsions; pulse gradually became weaker; died August 6. No autopsy.

Summary. The question of uremia was thought of; this was ruled out because of the low blood-pressure. Cerebrospinal lues was questionable, the spinal fluid being negative. Diagnosis: thermic fever. No blood data on this case.

Muich: male; aged forty-five years; laborer; habits irregular; entered 4.45 P.M. July 30, 1916; unconscious; temperature, 108.6° (rectal); pulse, 110; irregular respiration, 48; pupils reacting to light; no rigidity or convulsions; heart irregular, with no positive findings; reflexes sluggish; stool and urine involuntary; emesis greenish-colored fluid; blood-pressure (systolic), 100; developed alcoholic psychosis and marked hallucinations; became rational four days after entering, when he gave a history of previous attack of thermic fever. Recovered, leaving hospital August 6, 1916.

August 4. Urine, no data.

Blood: Urea nitrogen, 19 mgm. per 100 c.c.; uric acid, 3.3 mgm. per 100 c.c.; creatinin, 3 mgm. per 100 c.c.; sugar, 0.138 per cent.

Summary. Observation made when convalescent; retention not great. It will be noted that this case while it displayed severe clinical symptoms did not show in its blood chemistry any cause for making a fatal prognosis. His urea nitrogen was 19, uric acid 3.3, creatinin 3 mgm., blood-sugar, 0.138 per cent.; values slightly above normal. It must be remembered that his urinary findings were the same as those of the cases that died and the other cases that recovered, namely, albumin and casts.

Ship: white; male; aged fifty-three years; bartender; habits irregular; entered 6.15 P.M. July 31, 1916; unconscious; temperature 108.2° (rectal); pulse, 180; irregular; respiration 40, labored; systolic murmur of apex; contraction of heart poor; pupils contracted, reaction to light sluggish but equal; regained consciousness on the second day but remained irrational. Developed alcoholic

psychosis; on the fourth day a secondary rise in temperature of 104.2° (axilla) and generalized convulsions; died August 4, 1916. No autopsy. Note the marked retention in the laboratory report below:

August 3. Urine: Albumin, very faint trace; sugar, negative; acetone, negative; diacetic acid, negative; indican, moderate amount.

Blood: Urea nitrogen, 76 mgm. per 100 c.c.; uric acid, 14.8 mgm. per 100 c.c.; creatinin, 6.1 mgm. per 100 c.c.; sugar, 0.177 per cent.

Summary. Moderate number of epithelial cells and leukocytes; very occasional red blood cells; two finely granular casts found after a prolonged search; clinical signs good; retention high, attracting attention to fatal prognosis. Died one day later.

It was noted in this case that his original symptomatology did not attract our attention to any fatal ending. On the contrary he seemed in rather good shape. He entered on July 31. On August 3 his blood findings showed high retention, the most significant observation in the same being the creatinin value of 6.1 mgm. This observation was made from blood obtained in the morning. On the following morning he died.

Huth: white; male; aged forty-two; concrete worker; habits irregular; entered 6.15 P.M. July 29, 1916; unconscious; temperature, 108.2°; pulse, 170, regular; respiration, 36; generalized convulsions; labored breathing; pupils contracted; reaction sluggish; knee-jerks increased; toe signs questionable; developed second rise in temperature and alcoholic psychosis; regained consciousness the fourth day. Average blood-pressure, 120. Discharged, well, August 26, 1916.

August 2. Urine: Albumin, moderate amount; sugar, negative; acetone, small amount; diacetic acid, small amount; indican, moderate amount.

Blood: Urea nitrogen, 26 mgm. per 100 c.c.; uric acid, 9.6 mgm. per 100 c.c.; creatinin, 3.83 mgm. per 100 c.c.; sugar, 0.168 per cent.

August 12. Urine: Albumin, negative; sugar, negative; acetone, negative; diacetic acid, negative; indican, negative.

Blood: Urea nitrogen, 14 mgm. per 100 c.c.; uric acid, 3.3 mgm. per 100 c.c.; creatinin, 2 mgm. per 100 c.c.; sugar, 0.12 per cent.

Summary. Moderate number of coarsely and finely granular casts and occasional leukocytes; very occasional leukocyte. Retention not high; patient recovered, although clinical signs seemed bad. This is an interesting case in that his symptoms were very severe, and yet blood chemical findings at this time did not indicate much retention, an observation which was well borne out by later tests and the ultimate fate of this case. On the tenth day of his stay in the hospital his blood findings were practically normal and his recovery certain. He was discharged on the twenty-eighth day of his stay.

O'Connor: white; male; brewery worker; habits irregular; married; entered 4.40 P.M. July 31, 1916; unconscious; temperature, 110.5°; pulse, 160, thready in character; respiration, 44, labored; heart action very weak; pupils markedly contracted, no reaction; generalized convulsions, with marked spasticity; did not regain consciousness; lumbar puncture made and 35 c.c. of clear fluid under normal pressure was obtained; became progressively worse; died 8.20 P.M. August 1, 1916.

August 1. Urine: Specific gravity, 1015; albumin, moderate amount; sugar, negative; acetone, negative; diacetic acid, negative; indican, very large amount. Serious findings.

Blood: Urea nitrogen, 33 mgm. per 100 c.c.; uric acid, 1.32 mgm. per 100 c.c.; creatinin, 4.8 mgm. per 100 c.c.; sugar, 1.5 per cent.

Summary. Moderate number of coarsely granular casts and red blood cells; occasional leukocytes. Retention high; patient died same day. We might call attention to our observations above on Ship case as applying in all particulars to this case.

Fischer: white; male; aged forty years; plumber; married; habits irregular; entered 8.50 P.M. July 30, 1916; unconscious; temperature, 109° (rectal); pulse, 150, regular but weak; respiration, 30; breathing irregular and labored; pupils dilated, reaction very sluggish; knee-jerks sluggish; toe signs questionable; general spasticity of body present; became conscious on third day but irrational; developed convulsions of a generalized type. The blood-pressure taken at intervals was systolic, 109, diastolic, 87 mm. The white blood count was 10,000; Wassermann blood and spinal fluid negative.

August 2. Urine: Albumin, very large amount; sugar, negative; acetone, moderate amount; diacetic acid, moderate amount; indican, moderate amount.

August 8. Urine: Albumin, negative; sugar, negative; acetone, negative; diacetic acid, negative; indican, trace.

August 12. Urine: Albumin, negative; sugar, negative; acetone, negative; diacetic acid, negative; indican, very large amount.

August 2. Blood: Urea nitrogen, 32 mgm. per 100 c.c.; uric acid, 8.6 mgm. per 100 c.c.; creatinin, 4.1 mgm. per 100 c.c.; sugar, 0.162 per cent.

August 3. Blood: Urea nitrogen, 39 mgm. per 100 c.c.; uric acid, 9.8 mgm. per 100 c.c.; creatinin, 4.56 mgm. per 100 c.c.; sugar, 0.165 per cent.

August 4. Blood: Urea nitrogen, 39 mgm. per 100 c.c.; uric acid, 7.9 mgm. per 100 c.c.; creatinin, 4.47 mgm. per 100 c.c.; sugar, 0.18 per cent.

August 8. Blood: Urea nitrogen, 45 mgm. per 100 c.c.; uric acid, 7.1 mgm. per 100 c.c.; creatinin, 3.94 mgm. per 100 c.c.; sugar, 0.156 per cent.

August 8. Spinal fluid: Urea nitrogen, 44 mgm. per 100 c.c.; uric

acid, 0.88 mgm. per 100 c.c.; creatinin, 2.4 mgm. per 100 c.c.; sugar, 0.1 per cent.

August 10. Blood: Urea nitrogen, 55 mgm. per 100 c.c.; uric acid, 6.9 mgm. per 100 c.c.; creatinin, 5 mgm. per 100 c.c.; sugar, 0.174 per cent.

August 12. Blood: Urea nitrogen, 89 mgm. per 100 c.c.; uric acid, 8.2 mgm. per 100 c.c.; creatinin, 5 mgm. per 100 c.c.; sugar, 0.2 per cent.

Summary. Urinary findings indicated some marked renal disturbance, but not of the same importance as blood findings. Remarkable number of casts on last day of life. High retention, indicating probable fatal outcome. Patient died two days after creatinin reached 5 mgm. per 100 c.c. This was the most interesting case of our series, because it showed the typical high retention, gradually increasing, of all the constituents, finally reaching the fatal "creatinin" point of 5 mgm. Again, this patient lived fourteen days in practically an unconscious state, finally dying with the findings at autopsy above catalogued. It is also to be noted that the macroscopic and microscopic findings, particularly of the kidneys, showed nothing chronic, simply a cloudy swelling and possible passive congestion. This, of course, rules out the possibility of the blood retention in this case, being due to any pre-existing renal deficiency.

Postmortem examination of this case was made by Dr. D. F. Hochdoerfer, whose courtesy in demonstrating the gross changes we wish to acknowledge.

The complete autopsy report follows:

Color, white; sex, male; height, 5 feet 8 inches; weight, 130 pounds; hair, blond; eyes, gray.

External appearance: No evidence of external violence. Body emaciated.

Rigor mortis: Present.

Scalp: Normal.

Skull: Normal.

Membranes of brain: Thickened and adherent.

Brain: Watery and anemic.

Spine and spinal cord: Spine normal. Spinal cord at cervical section normal.

Pleural cavities: Adhesions right cavity.

Lungs: Pneumonic areas in right lower lobe. Bronchi filled with bloody, watery secretion. Right lung on section contained a large amount of watery exudate. All evidence of a bronchopneumonia present.

Intestines: Normal.

Liver: Fatty.

Spleen: Small.

Pancreas: Normal.

Kidneys: Parenchymatous and interstitial changes present. Cloudy swelling. Capsule slightly adherent.

Bladder: Normal.

Male genitalia: Normal.

Remarks: History, insolation July 30, with temperature 107°.

Pieces of the various organs were taken for microscopic examination, namely, brain, heart, spleen, pancreas, liver, and kidneys. The most definite changes were seen in the kidney structure. Here we had a typical picture of cloudy swelling without any of the well-marked changes of a preëxisting or long-standing degeneration.

The gross and microscopic changes in this case indicate a simple passive congestion of the kidneys and the usual absence of gross or minute manifestations as commonly seen in thermic fever.

We give below a summary of the blood and urinary findings in these cases.

BLOOD ANALYSIS										URINE ANALYSIS★									
CASE	DATE	TIME	TEMP.	PULSE	B.P.	HAEMOGLOBIN	HAEMATOCRIT	HAEMATOCENTRIFUGATION	REMARKS	SP. GRAVITY	ALBUMIN	SUGAR	ACETONE	LEUCOCYTES	EPITHELIAL CELLS	INDICAN	MICROSCOPICAL EXAMINATION	REMARKS	
O'Conner	8/1	DIED	33	132	40	50			RETENTION INDEX PATIENT DIED SAME DAY.	1.05	+	+	+	+	+	+	Moderate number of coarse granular casts and red blood cells. Occasional leucocytes.	FINDINGS SERIOUS	
Fischer	8/2		32	86	41	112			High retention index indicating probable fatal outcome. Patient died two days after creatine reached 5.0 mg-% per 100 cc.		+	+	+	+	+	+	Moderate number of granular casts and epithelial cells.	Urinary findings indicated some marked renal disturbance, but not same importance as blood findings.	
	8/3		39	98	45	105					+	+	+	+	+	+			
	8/4	DIED	39	79	44	100													
	8/6		45	71	39	45				1.04	+	+	+	+	+	+	Moderate number of epithelial cells leucocytes and fairly granular casts.		
	8/7		44	68	24	00													
	8/8		55	65	50	00													
Huth	8/1		89	82	50	40			Arrows at 10 h. Patient recovered a rough clinical signs seemed bad.	1.04	+	+	+	+	+	+	Very many granular casts and occasional leucocytes. Small number of casts in first day of life.	Remarkable number of casts on first day of life.	
	8/2		26	96	103	60				1.04	+	+	+	+	+	+	Moderate number of coarse and fairly granular casts and occasional leucocytes. Very occasional indican.		
Ship	8/5	DIED	76	140	61	100			Chest signs bad. Retention high, showing approach to fatal prognosis. Died one day later.	1.04	+	+	+	+	+	+	Moderate number of epithelial cells and leucocytes. Very granular and fairly granular casts. Small after prolonged search.		
Mulch	8/4		19	33	30	40			Observation made when comatose.										

* Not 100% of the amount
+ Moderately amount
+ Small amount.

★ All 10-15 life amount
+ Moderate amount
+ Small amount.

FIG. 1

For purposes of comparison we give a charted description of the blood changes in some of the well-known conditions in which the microchemical methods of Folin, Denis, Benedict, Lewis, Myers, and Fine have been worked out.

In passing it might be added that the blood-chemical analyses were made following the technic that has been elaborated by Folin and others. The blood was uniformly taken in the morning before nourishment was given. It was procured from one of the superficial veins on the forearm, received into potassium oxalate and defibrinated. A portion was precipitated at once with picric acid

for sugar and creatinin estimations, the balance being used for the urea-nitrogen and uric-acid determinations. For the sugar estimations we used the method of Benedict and Lewis;⁴ for the creatinin, the method of Folin;⁵ for the urea, the urease method of Marshall⁶ and Van Slyke;⁷ for the uric acid, the method of Folin⁸ modified by Benedict.⁹ In all cases we used the Hellige instrument in making our determinations.

THE CHARACTERISTIC BLOOD PICTURES IN GOUT, DIABETES & NEPHRITIS				UREA N, URIC ACID, CREATININE & SUGAR.
DISEASE	UREA N.	URIC ACID	CREATININE	SUGAR
	MGMS. PER 100 ^{cc} of BLOOD			PER CENT
NORMAL	12-15	1-3	1-2.5	0.08-0.12
GOUT		35-6		
MILD DIABETES				0.15-0.30
SEVERE DIABETES				0.30-1.10
CHRONIC NEPHRITIS	15-50	1-4	1-3	
UREMIC NEPHRITIS	80-300	4-15	4-34	0.10-0.20
THERMIC FEVER	UREA N 26-89	URIC ACID 6-14	CREATININE 3-6.1	SUGAR 0.15-0.20

FIG. 2

CONCLUSIONS. The study of these cases from the laboratory stand-point has been most instructive. Here we have in thermic fever a condition that is unquestionably analogous in its symptomatology to some form of uremia. Again, we have in the urinary findings a close resemblance to this condition. We found in the blood-chemical analyses of these cases high retention of the non-protein nitrogen constituents, indicating clearly a deficiency of renal function. In some cases the retention was high and the symptomatology not bad, yet these cases died. In other cases we found low retention and bad symptoms, and the patients uniformly recovered. Is this not then a truer guide to the exact status of the patient from the stand-point of prognosis than the data obtainable either from the clinic or urinary analysis? We do not wish by any means to insinuate that the whole course of any

⁴ Jour. Biol. Chem., 1915, xx, 61.⁵ Jour. Biol. Chem., 1913, xv, 487.⁶ Proc. Am. Soc. Biol. Chem., 1915.⁷ Am. Jour. Physiol., 1905, xiii, 45.⁸ Ibid., 1914, xix, 211.⁹ Jour. Biol. Chem., 1915, xx, 629.

case can be completely predicated upon the blood-chemical findings, but we do insist upon the great value of this work in this and allied conditions. The determination of the amount of creatinin in these cases has given us some figures which seem to bear out the contention of Myers and Lough¹⁰ that a percentage of creatinin that exceeds 5 mgm. per 100 c.c. of blood bodes ill for the patient. It will be noted that in the cases of O'Connor, Fischer, and Ship we had a creatinin value around or above 5 mgm. These three cases died. In the case of Ship at the time his blood was taken his clinical condition did not seem to be nearly as bad as that of Huth, yet the creatinin value of the former was above the so-called fatal point, whereas the latter had only a creatinin retention of 3.83 mgm. The case Ship, however, vindicated the prognostic value of a high creatinin retention, as he died on the morning following this determination, yet Huth, whose blood-creatinin was 3.83 at the time that his clinical condition seemed to point to a fatal ending, recovered, showing ten days later practically normal blood figures. Thermic fever can be added therefore to the set of conditions which with high creatinin value, 5 mgm. or over, can be said to offer a fatal prognosis. For all intents and purposes these figures in thermic fever may be construed as similar in their interpretation to those obtained in severe uremic nephritis.

TREATMENT. A word or two in regard to the treatment of these cases: tub baths, gradually cooling the water to ice bath until the patient's temperature was reduced to 104° or under; stimulation with camphor, strychnin, and digitalin, free elimination, proctoclysis, with normal saline solution. In general, symptomatic treatment.

We wish to extend our thanks to Mr. A. J. Blaivas for valuable assistance in the chemical analyses and to Drs. Irvin Schmidt and W. I. Smith, of the staff of the hospital, for their active coöperation.

THE CLASSIFICATION OF THE CHRONIC HIGH BLOOD-PRESSURE CASES.

By LOUIS M. WARFIELD, A.B., M.D.,

PROFESSOR OF CLINICAL MEDICINE, MARQUETTE UNIVERSITY MEDICAL SCHOOL,
MILWAUKEE, WIS.

THERE is no subject in medicine which, in the present age, has more vital interest to physicians than that of the chronic diseases of the circulatory system. Figures in all vital statistics have shown us that all affections of the circulatory and renal systems are definitely on the increase. "Arterial diseases of various kinds,

¹⁰ Arch. Int. Med., 1915, xvi, 536-546.